

Attorney Docket No. 71758/46943-CIP2
 U.S.S.N. 09/990,586
 Filed: November 21, 2001
 Preliminary Amendment
 Page 17 of 50

LC113:

5' GCTGCTGATCGTGAAAGAAAACCTTTGTGCCAGATCCACTG 3'(SEQ ID NO. 69)

LC125a:

5' CTGCAGAAACCAGGGCAATCTCCTCAGCTCCTG 3'(SEQ ID NO. 70)

LC123a:

5' CAGGAGCTGAGGAGATTGCCCTGGTTTCTGCAG 3'(SEQ ID NO. 71)

Figure 14 shows hOAT (humanized cH36-IgG1) constant region sequences of the light (Fig. 14A) (SEQ ID NO. 97) and heavy chain (Fig. 14B) (SEQ ID NO: 98). Figure 15 shows hFAT (humanized cH36-IgG4) constant region sequences of the light (Fig. 15A) (SEQ ID NO: 99) and heavy chain (Fig. 15B) (SEQ ID NO. 100). In each figure, the last amino acid residue of the framework 4 (FR4) variable region is connected to the first amino acid residue of the constant region for hOAT and hFAT.

IN THE CLAIMS

Please amend the claims as follows:

21. (Amended) The humanized antibody of claim 17, wherein the first CDR (CDR1) of the heavy chain hypervariable region is at least 95% identical to the CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8).
22. (Amended) The humanized antibody of claim 17, wherein the second CDR (CDR2) of the heavy chain hypervariable region is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101).

Attorney Docket No. 71758/46943-CIP2
U.S.S.N. 09/990,586
Filed: November 21, 2001
Preliminary Amendment
Page 18 of 50

23. (Amendment) The humanized antibody of claim 17, wherein the third CDR (CDR3) of the heavy chain hypervariable region is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10).

24. (Amended) The humanized antibody of claim 17, wherein the first CDR (CDR1) of the light chain hypervariable region is at least 95% identical to the CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2).

A12
25. (Amended) The humanized antibody of claim 17, wherein the second CDR (CDR2) of the light chain hypervariable region is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6).

26. (Amended) The humanized antibody of claim 17, wherein the third CDR (CDR3) of the light chain hypervariable region is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7).

27. (Amended) The humanized antibody of claim 19, wherein the first framework (FR1) of the heavy chain hypervariable region is at least 95% identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91).

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29. (Amended) The humanized antibody of claim 19, wherein the second framework (FR2) of the heavy chain hypervariable region is at least 95% identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91).

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31. (Amended) The humanized antibody of claim 19, wherein the third framework (FR3) of the heavy chain hypervariable region is at least 95% identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91).

Attorney Docket No. 71758/46943-CIP2
U.S.S.N. 09/990,586
Filed: November 21, 2001
Preliminary Amendment
Page 19 of 50

A15
33. (Amended) The humanized antibody of claim 19, wherein the fourth framework (FR4) of the heavy chain hypervariable region is at least 95% identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID No. 91).

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35. (Amended) The humanized antibody of claim 19, wherein the first framework (FR1) of the light chain hypervariable region is at least about 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

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37. (Amended) The humanized antibody of claim 19, wherein the second framework (FR2) of the light chain hypervariable region is at least about 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

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39. (Amended) The humanized antibody of claim 19, wherein the third framework (FR3) of the light chain hypervariable region is at least about 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

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41. (Amended) The humanized antibody of claim 40, wherein the fourth framework (FR4) of the light chain hypervariable region is at least about 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

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45. (Amended) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited, the antibody comprising on the heavy chain:

a) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

Attorney Docket No. 71758/46943-CIP2
U.S.S.N. 09/990,586
Filed: November 21, 2001
Preliminary Amendment
Page 20 of 50

- b) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),
- c) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),
- d) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),
- e) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),
- f) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and
- g) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID No. 79).

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46. (Amended) The antibody of claim 45 further comprising on the light chain,

- h) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),
- i) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),
- j) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),
- k) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),
- l) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),
- m) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

Attorney Docket No. 71758/46943-CIP2
U.S.S.N. 09/990,586
Filed: November 21, 2001
Preliminary Amendment
Page 21 of 50

n) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

A20 47. (Amended) The antibody of claim 45 further comprising the light chain constant sequence of Figure 14A (SEQ ID NO. 97) or Figure 15A (SEQ ID NO. 99).

48. (Amended) The antibody of claim 45 further comprising the heavy chain constant region of Figure 14B (SEQ ID NO. 98) or Figure 15B (SEQ ID NO. 100).

51. (Amended) A humanized antibody comprising on the heavy chain:

a) a first CDR (CDR1) identical to the CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

A21 d) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

e) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

f) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91); and

g) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID No. 91); and

on the light chain:

h) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

Attorney Docket No. 71758/46943-CIP2
 U.S.S.N. 09/990,586
 Filed: November 21, 2001
 Preliminary Amendment
 Page 22 of 50

i) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

A21 l) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

n) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

52. (Amended) The antibody of claim 51 further comprising the light chain constant sequence of Figure 14A (SEQ ID NO. 97) or Figure 15A (SEQ ID NO. 99).

53. (Amended) The antibody of claim 51 further comprising the heavy chain constant sequence of Figure 14B (SEQ ID NO. 98) or 15B (SEQ ID NO. 100).

A22 65. (Amended) A method of inhibiting blood coagulation in a mammal, the method comprising administering to the mammal, an effective amount of a humanized antibody or fragment thereof wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited, the antibody or fragment comprising on the heavy chain:

a) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

Attorney Docket No. 71758/46943-CIP2
U.S.S.N. 09/990,586
Filed: November 21, 2001
Preliminary Amendment
Page 23 of 50

c) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

e) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

f) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

g) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID NO. 91);

and on the light chain,

h) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

i) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

l) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

n) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID No. 79),

o) a light chain constant region which is at least 95% identical to the amino acid sequence shown in Figure 14A (SEQ ID NO. 97) or Figure 15A (SEQ ID NO. 99), and

Attorney Docket No. 71758/46943-CIP2
U.S.S.N. 09/990,586
Filed: November 21, 2001
Preliminary Amendment
Page 24 of 50

p) a heavy chain constant region which is at least 95% identical to the amino acid sequence shown in Figure 14B (SEQ ID NO. 98) or Figure 15B (SEQ ID NO. 100).

66. (Amended) A method of inhibiting blood coagulation in a mammal, the method comprising administering to the mammal, an effective amount of a humanized antibody or fragment thereof wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited, the antibody or fragment comprising on the heavy chain:

a) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

A22 b) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

e) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

f) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

g) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID No. 91);

and on the light chain:

h) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

Attorney Docket No. 71758/46943-CIP2
 U.S.S.N. 09/990,586
 Filed: November 21, 2001
 Preliminary Amendment
 Page 25 of 50

i) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

A₂₂ l) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

n) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

o) a light chain constant region which is identical to the amino acid sequence shown in Figure 14A (SEQ ID NO. 97) or Figure 15A (SEQ ID NO. 99), and

p) a heavy chain constant region which is identical to the amino acid sequence shown in Figure 14B (SEQ ID NO. 98) or Figure 15B (SEQ ID NO. 100).

STATEMENT ACCOMPANYING SUBMISSION OF SEQUENCE LISTING

Provided herewith is a Paper Copy of a Sequence Listing for the nucleotide and/or amino acid sequence(s) in this application. Upon entry of this amendment, each sequence has been assigned a separate identifier as required in 37 C.F.R. § 1.821(c) and 37 C.F.R. §§ 1.822 and 1.823. An amendment directing entry of the Paper Copy of the Sequence Listing into the specification is provided above.

Applicants further provide a Computer Readable Form (CFR) corresponding to the Paper Copy of the Sequence Listing provided herewith. Pursuant to 37 C.F.R. § 1.821(g), Applicants'